

Continuous positive airway pressure therapy in the management of hypercapnic cardiogenic pulmonary edema

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Abstract

Continuous positive airway pressure (CPAP) therapy or non-invasive ventilation (NIV) represent the first line therapy for acute cardiogenic pulmonary edema (CPE) together with medical therapy. CPAP benefits in acute CPE with normo-hypocapnia are known, but it is not clear whether the use of CPAP is safe in the hypercapnic patients. The aim of this study is to evaluate CPAP efficacy in the treatment of hypercapnic CPE. We enrolled 9 patients admitted to the emergency room with diagnosis of acute CPE based on history, clinical examination, arterial blood gas

analysis (ABG) and lung-heart ultrasound examination. We selected patients with hypercapnia (pCO₂ >50 mmHg) and bicarbonate levels <30 mEq/L. All patients received medical therapy with furosemide and nitrates and helmet CPAP therapy. All patients received a second and a third ABG, respectively at 30 and 60 min. Primary end-points of the study were respiratory distress resolution, pCO₂ reduction, pH improvement, lactates normalization and the no need for non-invasive ventilation or endo-tracheal intubation. All patients showed resolution of respiratory distress with CPAP weaning and shift to Venturi mask with no need for NIV or endo-tracheal intubation. Serial ABG tests showed clear reduction in CO₂ levels with improvement of pH and progressive lactate reduction. CPAP therapy can be effective in the treatment of hypercapnic CPE as long as the patients have no signs of chronic hypercapnia on ABG and as long as the diagnosis of heart failure is supported by bedside lung-heart ultrasound examination.

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Key words: Dyspnea; heart failure; blood gas analysis; hypercapnia; CPAP; lung-heart ultrasound.

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Introduction

Cardiogenic pulmonary edema (CPE) is among the most common causes of acute respiratory failure in the emergency department. It requires continuous positive airway pressure (CPAP) therapy or non-invasive ventilation (NIV) as first line therapy for its management together with pharmacological therapy (1). While the use of CPAP is consolidated and safe in normo/hypocapnic patients, NIV is believed to be safer in the hypercapnic population [1], although some studies have found no substantial differences in outcome between patients treated with CPAP and patients treated with NIV in this population [2]. Assuming that the pathophysiology of CO₂ accumulation in CPE is different from chronic obstructive pulmonary disease (COPD) exacerbation, we tested the efficacy of CPAP in patients with hypercapnic CPE who had received a diagnosis of CPE supported by integrated lung-heart ultrasound examination [3] and who had no blood gas analytical signs of chronic hypercapnia.

Materials and Methods

We enrolled 9 patients (7 females) taken to the emergency room of the C.T.O. hospital in Naples for acute dyspnea in red code for the severity of respiratory failure from August 2018 to January 2020.

Based on the history, physical examination, arterial blood gas analysis and lung-heart ultrasound examination performed

with Mindray M7 ultrasound machine by an emergency physician expert in lung ultrasound and echocardiography and according with the diagnostic pathway suggested by Carlino *et al.* [4], we made a diagnosis of acute CPE. We enrolled patients with hypoxia and partial pressure of carbon dioxide (PaCO₂) >50 mmHg. To avoid recruiting patients with chronic hypercapnia linked to COPD, we included only patients with HCO₃⁻ <30 mEq/L as suggested by Aliberti *et al.* [5]. All patients received medical therapy with furosemide (starting dose 40 mg) and nitroglycerine (starting dose 2 mg/h) as suggested by current guidelines [1] and helmet CPAP starting with a positive end-expiratory pressure (PEEP) of between 10 and 15 cmH₂O and an inspired oxygen fraction (FiO₂) of between 60% and 100%. All patients received a second and a third blood gas analysis at 30 and 60 min, an electrocardiogram, a chest X-ray and complete laboratory tests including brain natriuretic peptide (BNP) and C-reactive protein. The primary endpoints of the study were the resolution of respiratory distress, defined as dyspnea associated with cold sweats, use of accessory respiratory muscles and respiratory frequency greater than 25 acts per minutes, the reduction of PaCO₂, the improvement of pH, the maintenance of an arterial oxygen saturation ≥94%, the normalization of lactate levels, the non-need to use NIV or endotracheal intubation with mechanical ventilation. Other causes of dyspnea like pneumonia were ruled out during hospitalization. The study was conducted according to the principles of the Declaration of Helsinki. Data were analyzed using SPSS v. 21.0 (SPSS, Chicago, IL, USA). Continuous data are expressed as mean ± 1 SD or median and categorical variables as percentages. The variations of the means of continuous variables are shown using cartesian graphs.

Results

We enrolled 9 patients (7 females, 78%), 7 of them (78%) received diagnosis of heart failure with reduced ejection fraction while 2 of them had heart failure with preserved ejection fraction, 3 of them (33%) had atrial fibrillation. Table 1 shows the baseline characteristics of the study population. They are elderly patients presented as hypertensive CPE with high respiratory rate. BNP levels are high and so white blood cell count while the C-reactive protein has low values. All patients showed resolution of respiratory distress and normalization of lactates (on average 3.59 mmol/L at admission compared to 1.65 at 60 minutes) with switch to Venturi mask and no need for NIV or mechanical ventilation. Serial blood gas analysis showed progressive improvement of oxygenation (oxygen saturation was 86% on average at time 0 compared to 98% and 97% at 30 and 60 min), reduction in CO₂ levels (on average 65.2, 52.2 and 46.1 mmHg respectively at time 0, 30 e 60 min) and improvement of pH (on average 7.19, 7.28 and 7.36 respectively at time 0, 30 and 60 minutes) (Figure 1).

Discussion

PaCO₂ is strictly related to alveolar ventilation, being inversely proportional to it while it is poorly related to the characteristics of the alveolar-capillary membrane and to lung perfusion because CO₂ diffusibility is twenty times greater than that of oxygen and CO₂ is not bound to plasma proteins [6]. During COPD exacerbation

Table 1. Baseline characteristics of the study population.

Parameter (unit of measure)	Mean±SD(minimum-maximum)
Age (years)	78±6.5 (70-89)
Systolic blood pressure (mmhg)	190.55±17.58 (170-220)
Diastolic blood pressure (mmhg)	101.67±15.41 (80-125)
Heart rate (beats/minute)	102.89±23.78 (70-148)
Respiratory rate (breaths/minute)	34±4.79 (28-40)
Leukocytes (10 ³ /μl)	14.98±8.74 (8.39-32.66)
Neutrophils (%)	68.95±16.25 (41.6-87.4)
Red blood cells (10 ⁶ /μl)	4.62±0.75 (3.3-5.67)
Haemoglobin (g/dl)	12.19±2.43 (7.7-14.9)
Platelets (10 ³ /μl)	259.44±100.11 (161-481)
Troponin (ng/l)	32.75±24.64 (7.2-74.1)
Glucose (mg/dl)	233±58.54 (169-343)
Urea (mg/dl)	45.22±10.34 (33-62)
Creatinine (mg/dl)	1.07±0.35 (0.67-1.73)
Alanine transaminase (u/l)	29.89±11.63 (10-43)
Sodium (mmol/l)	140.55±2.92 (137-147)
Potassium (mmol/l)	4.3±0.34 (3.9-4.8)
C-reactive protein (mg/l)	10.63±6.71 (2.07-24.35)
	Median (minimum-maximum)
Brain natriuretic peptide (pg/ml)	752.3 (255.1-7178.3)

tion the increase of PaCO₂ is mainly due to reduced alveolar ventilation with incomplete expiration caused by airflow obstruction in the distal airways and to chest pump failure. During CPE the increase of PaCO₂ is mainly due to reduced alveolar ventilation caused by alveolar edema. During CPE, the increase of pulmonary capillary wedge pressure, caused by left ventricular diastolic dysfunction in both preserved or reduced ejection fraction heart failure, leads to interstitial edema that in the early stages causes

hypoxemia without modifying the exchange of CO₂ which on the contrary can also be reduced. With the worsening of the edema the transudate fills the alveolar cavities reducing their ventilation and, in some cases, causing complete atelectasis. This ultimately causes the worsening of hypoxia and the increase in PaCO₂. During COPD exacerbation a bi-level ventilation is necessary to reduce PaCO₂ because a positive end-expiratory pressure counterbalances the intrinsic positive end-expiratory pressure of COPD patients



Parameter (unit of measure)	Mean ± SD		
	T0	T30	T60
Arterial oxygen saturation (%)	86.3 ± 18.01	98.18 ± 1.68	97.48 ± 1.47
Fraction of inspired oxygen (%)	60.11 ± 19.75	71.11 ± 22.05	60 ± 23.98
pH of arterial blood	7.19 ± 0.10	7.28 ± 0.09	7.36 ± 0.05
Partial pressure of CO ₂ (mmHg)	65.22 ± 13	52.22 ± 7.63	46.11 ± 5.77
Partial pressure of O ₂ (mmHg)	79.11 ± 46.95	143.55 ± 116.11	98.89 ± 49.58
Bicarbonate (mmol/L)	24.54 ± 2.27	24.49 ± 3.24	25.89 ± 2.97
Lactate (mmol/L)	3.59 ± 2.64	2.25 ± 2.44	1.65 ± 1.22

Figure 1. Arterial blood gas analysis at time 0, at 30 and 60 min with graphics on variation of pCO₂, oxygen saturation, pH and lactate.

and a pressure support reduces the work of the respiratory muscles to win airway obstruction, helping the patient in the inspiratory phase. During CPE a continuous positive end-expiratory pressure is sufficient also in reducing PaCO₂ because it improves alveolar ventilation by allowing the recruitment of imbedded alveoli, promoting the reabsorption of edema and improving cardiac performance. Obviously, this type of approach requires accuracy in diagnosis. In addition to history and physical examination, blood gas analysis and point of care ultrasound are essential in the differential diagnosis in the early phases. Patients with acute on chronic respiratory acidosis have significantly higher bicarbonate levels than patients with acute respiratory acidosis. With a retrospective analysis of a study carried out in the emergency department on patients with CPE treated with CPAP [7], Aliberti *et al.* showed that the bicarbonate cut off to distinguish patients with acute on chronic hypercapnia from those with acute hypercapnia was 30 mEq/L. Patients with pulmonary edema and bicarbonate levels >30 mEq/L treated with CPAP had a worse clinical outcomes in comparison with patients with bicarbonate levels ≤30 mEq/L with a higher rate of transition from CPAP to NIV [5]. If, on the one hand, blood gas analysis gives us information on the presence of chronic hypercapnia, the integrated lung-heart ultrasound confirms or not the diagnosis of acute cardiogenic pulmonary edema. In case of pulmonary edema a diffuse bilateral lung interstitial syndrome (confluent B-lines that configure a “white lung” picture) is present [8]. Heart ultrasound examination with the evaluation of left ventricular ejection fraction, left atrial dimension and left ventricular diastolic function confirms the cardiogenic origin of pulmonary edema with an accuracy of 96% [3,4,9]. This approach ultimately distinguishes interstitial syndrome resulting from cardiac dysfunction from all other forms of widespread interstitial syndromes: acute respiratory distress syndrome (ARDS), pulmonary fibrosis, bilateral interstitial pneumonia, bilateral pulmonary metastasis [10]. The most important limitation of this study is the sample size which is low although it must be taken into account that the cases of hypercapnic CPE represent about 10% of the cases of CPE [7], on which we have made a further selection based on the bicarbonate levels on the first blood gas analysis. Moreover, all patients presented as hypertensive CPE. However, further studies with larger samples are needed.

Conclusions

Helmet CPAP can be used to treat hypercapnic CPE as long as there is an accurate selection of the patient who must not have

starting bicarbonates greater than 30 mEq/L and must have a diagnosis of acute heart failure supported by integrated lung-heart ultrasound examination.

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